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Scientific Opportunities and Investigator Competencies

The Challenge

Opportunities in health-related research abound. However, the fields in which the opportunities occur are broad and changing quickly. These extraordinary opportunities require the preparation of individuals who are creative, independent, and yet capable of working collaboratively.

For organizations involved in the development of the scientific talent pool, such as the National Institute of Dental and Craniofacial Research, the challenge is to create a diverse, well-trained, versatile and flexible workforce. What is needed is a workforce that can realize the *full potential* of the scientific opportunities that will continue to emerge in the coming years.

Following their opening remarks, Panel co-Chairs Joseph P. Martin and Charles Bertolami called upon each member of the Blue Ribbon Panel to respond to the questions presented to them in advance of the meeting:

- *What are the most exciting scientific opportunities that have emerged in recent years or that we may anticipate in the next few decades?*
- *What new skills and competencies must scientists acquire in the coming years in order to respond to emerging or anticipated scientific opportunities?*

What follows is a brief summary of their observations.

Question 1: Scientific Opportunities in the 21st Century

Panel members noted that developments in science move too rapidly to identify specific areas of opportunities. Rather, they focused on identifying major trends of interest to the Institute. They agreed, that health-related research at the start of the 21st Century would be quite unlike that which we observe today. In their view, there will be a rise in *interdisciplinary studies* in the coming years. There will be a resurgence of *functional analyses* following an extended period of "reductionist" research. Furthermore, there will be greater emphasis on *applied research*, which includes translational and clinical research, population-based studies, domestic and international collaborations, and health services research.

Admittedly, there is a degree of ambiguity and uncertainty in the new formulations and new alignments to be expected in the coming years. Nonetheless, as Panel co-chair Dr. Charles Bertolami noted in his opening remarks:

> "Our task is to determine what it is going to take in order to keep the ball in play in the oral health sciences."

Interdisciplinary Research

Scientists active today were for the most part trained in a particular discipline. Each of those disciplines has made dramatic contributions to the understanding and treatment of disease. However, many of the health challenges of the 21st Century are going to be beyond the expertise and training one can receive in any particular discipline. As a result, scientists will need to acquire a broader mix of skills and must learn to work collaboratively in order to make inroads in the health questions that remain to be addressed.

Panel member, Dr. Norman Anderson, Associate Director of the NIH Office of Behavioral and Social Science Research, reviewed his experience since joining the National Institutes of Health. One of his primary tasks was "to develop a way of talking about the relevance of behavioral and social sciences research" to the "largely biomedical" orientation of the NIH. Dr. Anderson observed that he needed a way to talk about how the social and behavioral sciences fit into the organization. He began to work with the concept of "levels of analysis." As Dr. Anderson noted, "This is not a new expression…but I don't think it has been fully elaborated to express the true promise of this perspective in health."

Dr. Anderson offered five "levels of analysis": (i) social/environmental, (ii) behavioral/ psychological, (iii) organ systems, (iv) cellular, and (v) molecular.

"The social/environmental level includes such variables as stressful life events, social support, economic resources, neighborhood characteristics, and environmental hazards. The behavioral/psychological level may include emotion, cognition, memory, dietary practices, stress coping styles, and tobacco use. The organ systems level of analysis includes the cardiovascular, endocrine, immune, and central nervous systems and their outputs. On the cellular level, variables include receptor number and sensitivity, dendritic branches, synapse number, and electrical conductance. Finally, the molecular or genetic level includes such variables as DNA structure, proteins, mRNA, and transcription factors." N. Anderson, Annals of NY Academy of Sciences, p. 565, 1998.

According to Dr. Anderson what is needed is "several generations" of scientists who are trained in one discipline but are then able to speak across disciplinary lines. To do multi-level research, it is not necessary "to turn a microbiologist into a sociologist." But these specialists will need to have sufficient familiarity with the other disciplines in order to develop collaborations. Dr. Anderson offered the following example of how we will need to think about fostering these levels of collaboration.

"Behavioral and social scientists have identified significant behavioral and social predictors of various health outcomes. Molecular biologists looking at some of the same health problems -- such as lung cancer -- have found significant molecular predictors of lung cancer. [We know that] the P-53 gene predicts lung cancer and smoking and certain chemicals in cigarette smoke predict lung cancer. They're working in an interactive way, rather than a parallel way…Some of us need to take that work, look across disciplines, and begin to develop multi-level theories and multi-level methods…to reach a full understanding of the causes of illness and to develop the best preventative and treatment approaches."

There are many other examples in which the research opportunities are characterized by the unique blend of disciplines, techniques and approaches. Scientists have shown that stress affects the functioning of the immune system. Even progression of HIV seems to be accelerated in individuals who are under chronic stress.

Of course, many scientists and engineers have been working cooperatively and productively in certain areas of clinical medicine. What is changing, according to Blue Ribbon Panel member Dr. Linda Griffith, Professor of Chemical and Bioengineering at MIT, is the "involvement of the engineer in the basic science of molecular cell biology." Unlike a physicist or a biophysicist who

would focus on molecular interactions, the bioengineer looks at the way a molecule actually works in the system.

According to Blue Ribbon Panel member, Dr. Bruce Baum, NIDCR Division of Intramural Research, some scientists involved in oral health research have already moved into translational and clinical research at the interface of biomaterials development and tissue engineering. Bioengineering is an interdisciplinary field aimed at enhancing the development of natural and synthetic diagnostics, therapeutics, and biomaterials for repair, regeneration, restoration, and reconstruction. As Dr. Baum noted:

"Tissue engineering offers an extraordinary opportunity for NIDCR. The areas that NIDCR might capitalize on in the future include new organ development, such as artificial salivary glands as well as bone regeneration and soft tissue repair."

Other areas of significant promise, in Dr. Baum's estimation, include oral biofilm manipulation; the molecular and developmental neurobiology of pain; and gene therapy. Research in each of these areas will require an "appropriate mix of individuals and understanding of disciplines" in order to respond to these research opportunities, according to Dr. Baum.

Some researchers have already taken the first steps toward creating “semisynthetic” organs that can be used to repair or replace damaged or diseased parts of the body. It is theoretically possible to engineer large, complex organs such as livers, kidneys, and teeth. As Mooney and Mikos note in their recent article: “Even the heart is a target for regrowth.”[4]

Dr. Enriqueta Bond, a member of the Blue Ribbon Panel and President of the Burroughs-Wellcome Fund, noted that private foundations have recognized the increasing role of interdisciplinary research in the biosciences. In fact, following a recent meeting of several philanthropic organizations, scientists can expect greater support for research "at the interfaces of science," according to Dr. Bond.

In offering some closing comments, Dr. Gladys Escalona of the University of Puerto Rico and a Blue Ribbon Panel member, observed that:

"…Science will need individuals who are aware of the benefits of collaborative or transdisciplinary work, and not only 'aware' but also willing to do what is needed to become part of a large group of scientists and to be effective in collaborative work."

Genomics and Functional Genomics

Another theme that emerged during the course of the Panel's deliberations is the impact of genetics research on the future direction of research.

The driving force behind many scientific discoveries in the future, according to the Panel, will be the Human Genome Project and the many other studies of microbial and mammalian genetics. These international collaborative efforts will provide detailed information about genes and genomic structures in a number of organisms. Not only will scientists ultimately understand how genes are structured, but they will also understand how genes work *with* each other and how the proteins produced by the genes interact to cause and produce the structure and function of each of the cells in our bodies.

[4] DJ Mooney and AG Mikos, “Growing New Organs”, Scientific American, April 1998, pp. 59 –65.

As Panel co-chair, Dr. Joseph Martin, observed:

> "The reductionist approach to science has been extraordinarily successful. Much of what we know has been derived from understanding cells and molecules -- indeed, atoms. But somebody has to think about how those things come together again. Whether one is thinking about cancer, intracellular communications, or the psychoneuroendocrine system, someone has to begin to pay attention to what is going to emerge as the new molecular physiology."

The Panel recognized that scientists are already examining genetic data to achieve a molecular understanding of body processes in the area of "craniofacial morphology." From their background readings, the Panel learned, for example, that Dr. Bjorn Olsen, Professor at Harvard Medical and Dental Schools, told participants at a 1998 NIDCR-sponsored symposium[5] that 50 years of sophisticated research in collagen protein chemistry and on collagen secretion and molecular assembly have led to important advances in understanding craniofacial skeletal morphogenesis. Postgenomics research has also led directly to the growth of bioinformatics -- that is, the development of large and complex databases for purposes of biomedical research and development. Scientists need to know today how to handle data, how to store it electronically, how to mine the data and how to use the information to conduct experiments.

The Panel learned, furthermore, that Dr. Robin Winters, Professor at the Institute of Child Health, London, at the same conference[6] noted that the ultimate goal of studying craniofacial anomalies is to define and predict normal facial development: "to predict an individual's facial phenotype from their genotype." To that end, Dr. Winters has accumulated an enormous database that can be used to explore the combinatorial assembly of gene expression in craniofacial morphology. The "London Dysmorphology Database" provides a useful example of the role of bioinformatics in research and development. Since 1983, that database has recorded 3,100 entries. About 1,700 appear to be single-gene syndromes, while 600 are thought to be sporadic syndromes. As Dr. Winters said at the 1998 NIDCR symposium: "Scientists in 1998 know of 197 human craniofacial disorders from which the genes have either been mapped or found, compared with 53 disorders in 1996. Of the 197 disorders now identified, 88 have had the gene mapped and 109 have defects found in 81 genes."[7] Those numbers are even larger today!

Achievements in biology and medicine in the 21st Century will require substantial investment in bioinformatics. In 1998, the White House Office of Science and Technology Policy convened a workshop on the topic and participants concluded, "…bioinformatics will be critical not only to the future of genomics but to most areas of biological and biomedical research."[8] Just one year later, the NIH Working group on Biomedical Computing issued a report under the auspices of the NIH Advisory Committee to the Director. The authors of that report noted that researchers are spending less time in their "wet labs" and more time on computation. As the report noted: "The biomedical community is increasingly taking advantage of the power of computing, both to manage and analyze data, and to model biological processes".[9]

From their review of these and other reports, the Blue Ribbon Panel concluded that computation is becoming an enabling technology in biomedicine. It seems clear that scientists in the coming years will have to be conversant with molecular biology and the meaning and use of the

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[5] NIDCR, Toward an Understanding of Craniofacial Morphogenesis, Office of the Director, November 1998.
[6] Ibid.
[7] Ibid.
[8] National Science and Technology Council, Bioinformatics in the 21st Century, White House Office of Science and Technology Policy, http://whitehouse.gov/WH/EOP/OSTP/NSTC/html/bioinformaticsreport.html
[9] NIH, "The Biomedical Information Science and Technology Initiative", prepared by the Working Group on Biomedical Computing, Advisory Committee to the Director, June 1999, http://www.nih.gov/welcome/director/060399.htm

information emerging from human, animal model, and microbial genome projects in order to assure the success of their endeavors.

Applied Research

A number of members of the Blue Ribbon Panel pointed to the growing importance of "applied research" in the biosciences. This includes domestic and international collaborative translational and clinical research, population-based studies, epidemiology, health promotion, and health services research.

Approaching the topic from the point of view of an epidemiologist, Panel member Dr. Raymond Greenberg, Vice President for Academic Affairs and Provost of the Medical University of South Carolina, put it this way:

"There is a whole vista opening up in the understanding of the genetic basis for diseases with complex susceptibility patterns of inheritance. To me, a classic example is Alzheimer's Disease. We are just beginning to scratch the surface in understanding the susceptibility markers. As the Human Genome project produces more markers…there will be opportunities to look not only at the genetic basis of the disease, but more importantly at the gene/environment interactions…the relationship between exogenous factors and the endogenous factors in terms of disease susceptibility."

As an example of the extent of demand for interdisciplinary research, Panel members referred to the results of a workshop on "head and neck cancer" sponsored by NIDCR earlier in the year. At that workshop, participants explored such issues as the etiology and pathogenesis of head and neck cancer, and the clinical research that will address innovations in imaging, diagnosis therapeutics, and pathogenesis treatments. Participants noted that cancers in general are genetic diseases in which progression of genetic aberrations are involved in the process of carcinogenesis, subsequent invasion, and metastasis. However, research is rapidly increasing which explores the genetic bases for the regulation of cell differentiation, proliferation, motility and apoptosis, as are the technological advances to assess these processes. The recommendations from the NIDCR workshop on head and neck cancer were designed to guide the development of "a multidisciplinary collaborative approach to reducing the mortality and morbidity associated with head and neck cancers."[10]

The picture that emerges is one of carefully assembled, carefully evaluated data for clinical care.

Panel member Dr. Howard Bailit of the University of Connecticut Health Sciences Center, concurs. Clinical researchers of the future will need to be familiar with population-based research: "They will need to have some idea of how to collect, analyze, and interpret information on large groups of people." But Dr. Bailit was quick to include the notion of "international collaborative research." There are many reasons to expect a "major blossoming" of this sort of research.

"We live in a global village and we are a part of a much larger system. I think there are many opportunities, especially for individuals involved in population-based care, to begin to think more broadly than their local community -- whether they are behavioral scientists, epidemiologists, clinical researchers or the like."

[10] NIDCR, Head and Neck Cancer Workshop, February 1999, Office of the Director.

Dr. Baum also endorsed the notion of the emergence of health promotion studies in the coming years. The operative concept for Dr. Baum was "access."

"My profession has done wonders for a portion of the population in the United States…Dentistry has made remarkable contributions in terms of addressing tooth decay. But there is a very specific opportunity to focus on the development of novel biopharmaceuticals in such a way that an auxiliary health worker could eventually distribute a mouth rinse to children to control populations of bacteria in their teeth. I don't think this is terribly far-fetched."

Dr. Bailit observed that scientists have already produced new sets of interventions and diagnostic treatments. Having knowledge of these approaches is one thing, according to Dr. Bailit, "Their effective application is another issue." Dr. Bailit anticipates that health services research will become increasingly important in the coming years. This is the science of the dissemination, evaluation, and effective implementation of emerging treatments and technologies.

A number of Panel members supported the notion that opportunities in "applied research" in these various forms will emerge in the coming years. Dr. Escalona added a cautionary note: The internationalization and globalization of population-based studies will also require scientists to attend to the unique characteristics and needs of the world's diverse populations and communities as they pursue applied studies in the coming years.

Question 2: Investigator Competencies

Following their discussion of emerging research opportunities, the Blue Ribbon Panel turned their attention to the issue of "competencies".

Panel members offered a list of skills that most scientists would need to acquire, given the anticipated direction of health research. In addition, two other themes emerged. The first of these involved the need to "prepare" individuals from more diverse cultural backgrounds to pursue training opportunities in health research. The other theme addressed the crucial role of research-intensive academic environments in facilitating skill acquisition and career formation in the sciences.

Each of these topics is addressed below.

Core Competencies

In the coming years, health-related research will be more interdisciplinary, more "molecular", and more focused on biological processes. As a result, there will be greater emphasis on the application of research findings to health promotion and disease prevention -- locally, nationally, and globally. The probable direction that health research will take suggests that scientists will *at a minimum* need to be familiar with the knowledge and methods of a wider variety of "disciplines" than is presently the case. Blue Ribbon Panel member Dr. Lawrence Tabak of the School of Medicine and Dentistry at the University of Rochester, offered the following examples: molecular biology, bioengineering, biomathematics, information science, physiology, and biochemistry. Other candidate subject areas offered by members of the Blue Ribbon Panel include endocrinology, quantitative analytic skills, team/collaborative skills, ethics and bioethics training, oral and written communication skills, management skills, entrepreneurship and knowledge of technology transfer approaches.

Many factors will shape the skill set sought by individual scientists. However, scientists will basically need to be full members of research teams in the future. Panel member Dr. Marjorie Jeffcoat of the University of Alabama School of Dentistry, commented:

"We want 'inquiring minds'. Whether they want to know about biological chemistry, whether they want to do postgenomics, whether they want to do bioengineering, it does not matter. They have got to have that feeling that they just want to dig their fingers into a problem."

Dr. Phyllis Beemsterboer of the UCLA School of Dentistry and a member of the Blue Ribbon Panel agreed, but stressed the importance of acquiring what she termed a "collaborative skill set".

"We're going to need a collaborative skill set that takes collaborative thinking as the basis for whatever areas we move into. The collaborative skill set will include ethical awareness."

Panel member Dr. Vincent Rogers, Associate Administrator of the HRSA Bureau of Health Professions, also views ethical awareness as a "core competency".

"As you look at research projects, for example, are underrepresented minorities involved? Have issues of consent been addressed? What comes to mind, of course, are the lingering issues from the Tuskegee experiment."

Dr. Frank Talamantes of the University of California at Santa Cruz raised the question of whether rapid developments in the health sciences have placed new pressures on young scientists with respect to grant writing. He observed that young assistant professors and postdoctoral research scientists are often naïve about writing grants. Few of them have been taught how to write competitive grant applications. A fundamental criticism is the lack of readiness among all too many clinicians to write research grants.

A number of Panel members suggested that a "positive mentor" is needed for students to "get started" in developing the mix of skills that they will need to succeed in contemporary science. Faculty provide the guidance that students need in their role as mentors and models. This observation prompted Dr. Tabak to comment that the need for a new and different skill set is not restricted to newly minted investigators.

"We have to retool a whole generation of very willing and able faculty who will be left behind if we don't consider their needs."

Students and faculty alike have got to be ready to "pivot" during the course of their careers, according to Dr. Jeffcoat:

"All of us have to be able to change our skills, work with new sets of people, and to teach our students that this is a good thing."

Fostering Talent Flow

As the Blue Ribbon Panel identified key core competencies, it became clear that there was a prior question. That question involved the development of the fundamental set of science and math skills that permit individuals to even *consider* pursuing a career in research.

Dr. Rogers noted:

"There are tremendous disparities in the representation of minorities in the health professions. We can only address that problem by introducing major shifts in our policies and programs."

The Health Resources and Services Administration recently introduced a program that focuses resources at the precollege level, according to Dr. Rogers. That program, "Kids into Health Research," aims to create competitive individuals from disadvantaged backgrounds -- to prepare them for undergraduate school and ultimately for a career in the health professions.

Dr. Talamantes seconded the notion that programs need to focus on pre-college recruitment. He added, however, that this is not as easy a process as it may seem. He suggested that the scientific community should make a greater effort to attract students into science who have made it through high school so we wouldn't lose that talent in the higher education process. The early years of baccalaureate education, according to Dr. Talamantes, are a time when the flow into science could be greatly diversified and the numbers expanded.

Dr. Rogers mentioned that the National Research Council, in 1994, issued a report on Meeting the Nation's Needs for Biomedical and Behavioral Scientists.[11] In that report the authors concluded that the outlook for researchers was favorable in a number of areas including oral health research. Yet, numerous articles have pointed out "both preventive medicine and primary care have substantial physician workforce shortages…and fewer physicians entering research careers." Dr. Rogers then described a number of steps that the Health Resources Administration has taken in recent years to connect "access" to "research" through the "education-service-research linkage." These include expanding the program of National Research Service Awards, promoting the development of primary care faculty through Title VII fellowships, and encouraging diversity.

"To enlarge the number of underrepresented minorities who are competitive for entry into health professions schools and programs, health professions institutions should create partnership arrangements with undergraduate schools, school districts, and with appropriate community-based organizations."

Dr. Rogers also mentioned the HRSA/HCFA Interagency Oral Health Initiative launched in 1999 that coordinates dental health programs to "promote the application of dental science and technology towards reducing and managing common oral diseases."

"It has been stated that tooth decay is the most prevalent chronic childhood disease in the United States, where access to dental care for the poor is lacking, often even when they are covered by Medicaid…HRSA and the Bureau of Health Professions will continue to strive to improve the efficiency and effectiveness of health care delivery and research, including health promotion and disease prevention activities. The emerging scientific opportunities will drive the research of the future to be more responsive to the needs of the public."

As Panel co-chair, Dr. Joseph Martin observed at the conclusion of the discussion:

"Our society is emerging demographically into a multi-cultural, multi-ethnic one. How do we face health care issues in that regard? How do we face the educational opportunities?"

[11] NRC, 1994, *op. cit.*

The Training Environment

Another theme that pervaded Panel discussion of scientific competencies involved the critical role that the "research-intensive" academic environment plays in promoting the development of a skill set in health research. As Dr. Jeffcoat put it: "The goal of the faculty is to train people who are better than they have ever been." Recognizing that dental, craniofacial and oral health research is a full partner in the health sciences, Dr. Baum added:

> "Our goal should be to get the best people to do the best research, to ask the toughest and best questions, to make oral health a right and not a privilege of everyone in this country."

Nonetheless, the Panel acknowledged that students preparing for a career in health-related research do best if they acquire the distinctive competencies that are needed in a research-intensive academic environment. Mentors, role models, and opportunities to participate in interdisciplinary research will all be needed. Dr. Bailit put the question this way:

> "Do we have an infrastructure in our dental education system that will promote, foster, and allow us to develop the kinds of training programs that we all want?

Blue Ribbon Panel member Dr. John Howe, President of the University of Texas Health Sciences Center at San Antonio, observed:

> "I think a lot of the training [we see] is going to be influenced by the resources that are available. I think a lot of the resources are going to be available based upon the degree to which we can capture the hearts and minds of those who are willing to fund it…What is the vision? What do we in oral health want to see in terms of the outcomes in the future?"

In the early 1990s, Dr. Howe served as Chair of the Committee on the Future of Dental Education organized by the Institute of Medicine.[12] During the course of the project, committee representatives visited 11 university campuses to explore the research opportunities for students in dental schools. Dr. Howe referred the Blue Ribbon Panel to the report whose recommendations included suggestions for expanding dental school involvement in research. Dr. Howe cautioned the Blue Ribbon Panel to keep in mind the “reality of the environment.” Something must be done to change the environment in order to create “the next generation of researchers.”

Dr. Greenberg echoed this theme by suggesting that there are two aspects of the "critical mass" issue in research training and competency development. The first is that health scientists -- no matter what their specialty -- must be well integrated with the work on the rest of their campuses.

> "There is a great advantage in developing relationships on campus in terms of leveraging resources."

Dr. Greenberg added that there are ways to augment and strengthen the research environment of each campus. Creating partnerships with nonacademic organizations and laboratories can form pools of mentors. Speakers can be brought to the campus and faculty given the opportunity to enhance their research skills through sabbatical arrangements.

[12] MJ Field (Ed.), 1995, *op. cit.*

Dr. Rogers noted that HRSA and specifically the Bureau of Health Professions are “directly involved” in meeting the challenges that would enhance the integration of medicine with the health care system at all levels, and that would continue testing the alternative models of dental education, practice and performance.

Rather than solving the problems confronting dental education, Dr. Bailit suggested that the goal was to make "incremental improvements" in training programs as they currently exist. Panel members differed with respect to their suggestions for "promoting" research intensity on university campuses. They agreed, however, that there is an important opportunity for the National Institute of Dental and Craniofacial Research in this area. The Institute should encourage research training and career development in those settings that provide the experience students will need if they are to tackle the most challenging research questions in the coming years.

In summary, the Blue Ribbon Panel on Research Training and Career Development to Meet Emerging Scientific Opportunities of the 21st Century identified several areas of rapid scientific advancement and promise. These areas can be generally described to include “interdisciplinary research”, “genomics and functional genomics” and “applied research”. Furthermore, anticipated advances in research will require that scientists of the future be prepared in a wider variety of subdisciplines than is currently the case. To assure that scientists are available with the requisite experiences and skills, education and policy leaders will need to enhance current efforts to recruit, train and retrain specialists capable of advancing health research in the coming years.

One way to think about this issue is to imagine a cube whose axes represent a three-dimensional portrait of “targets of opportunity” for leveraging resources to produce the scientific talent that will be needed in the coming years. One dimension represents the five levels of analysis described by Dr. Anderson earlier in the meeting: social/environmental, behavioral/ psychological, organ systems, cellular, and molecular science. The six scientific priority areas of the NIDCR Strategic Plan represent a second dimension. The levels of research training and career development (precollege/college, professional, postgraduate/postdoctoral, and midcareer) represent the third dimension of this cube. (See Appendix C, Model for “Targets of Opportunity”.) The target opportunities reside at the interface between these three dimensions, recognizing that the key to all this is the availability of adequate financial and human resources. Some research training and career development opportunities and strategies that respond to these emerging needs are described in the chapter that follows.